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A Review Article On Cilnidipine And Its Evaluation Methods.

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Abstract

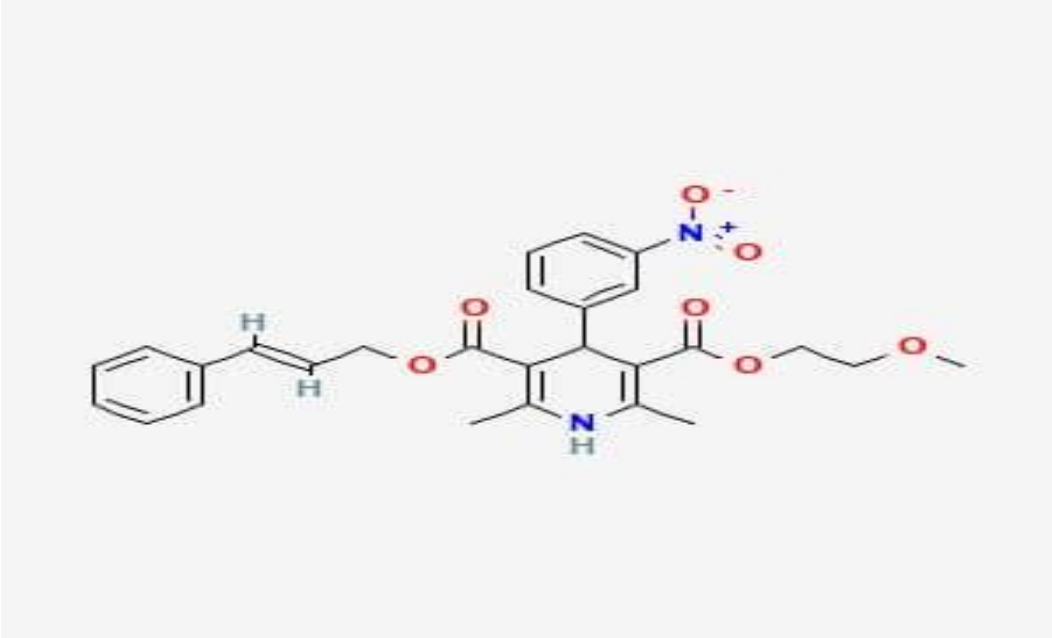
Cilnidipine is a medication which are used for the treatment of hypertension (The drug Which lowers the blood pressure). The Cilnidipine is a BCS Class-II drug.Cilnidipine is a medication which are used for the treatment of hypertension (The drug Which lowers the blood pressure). The Cilnidipine is a BCS Class-II drug.It is a novel dihydropyridine calcium antagonist and its calcium antagonistic activity last for a long time more than other drugs like Nifedipine and NicardipineThe objective of the study is to get knowledge about formulation and evaluation parameters of orodispersible tablets of Cilnidipine. The objective of this work was to enhance the solubility and dissolution rate for rapid onset of anti-hypertensive action of cilnidipine.

Keywords- Cilnidipine, Orodispersible,

Introduction

Cilnidipine is a class of calcium channel blocker. The drug lowers blood pressure by relaxing blood vessels, which makes the heart more efficient at pumping blood throughout the body.Cilnidipine has been also used for the treatment of hypertensive-associated vascular disorders. The drug can be given in adult about 40 to 80 mg once daily." Cilnidipine has a very low solubility (BCS Class-II drug Low solubility high permeability) and compliance to the medication is always very poor.Orodispersible tablets are the medications that disintegrates rapidly generally in seconds when put on the tongue because it contains mainly medicinal substances in the solid dosage form.It is also known as orally disintegrating tablet or orally dissolving tablet. The drug available for a limited range of over-the-counter and prescription medications. Itdiffer from traditional tablets, they are designed to be dissolved on the tongue rather than swallowed whole.The concentration of a solute in a saturating solution at an equilibrium temperature is known as solubility. One technique for enhancing the dissolving of poorly soluble drugs with a low absorption rate is solid dispersion. Solid dispersion is defined by Chiou and Liegeman as "the process of

producing eutectic mixtures of pharmaceuticals with water soluble carriers by melting of their physical mixtures.



Molecular Formula : C27H28N2O7

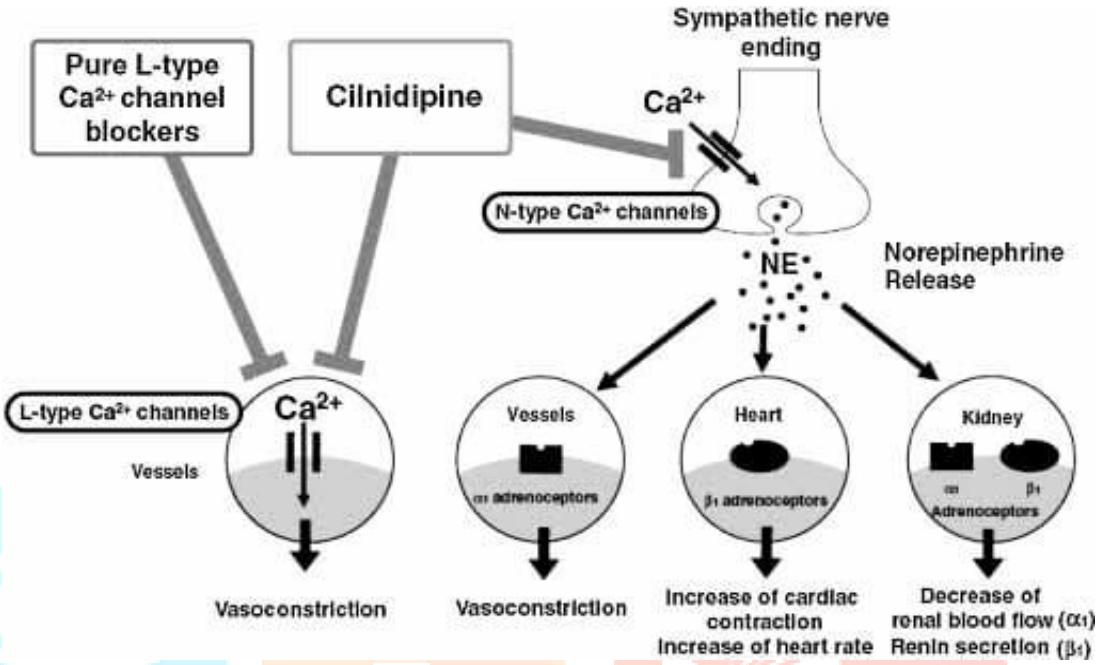
Molecular Weight : 492 gm/mol

Physico Chemical Properties :

- Molecular Formula : C27H28N2O7
- Density : 1.240±0.06 g/cm3,
- Melting Point : 97-99°C,
- Boling Point : 652.6±55.0 °C,
- Flash Point : 335.182°C
- Solubility : H2O: ≤2mg/mL
- Vapour Presure: 0mmHg at 25°C,
- Appearance : Yellow

Mechanism of action :

It acts on L-type calcium channels of blood vessels by blocking incoming the calcium ions and suppressing contraction of blood vessels & therefore responsible for reducing blood pressure. Cilnidipine is also works on N-type calcium channel located at end of the sympathetic nerve & inhibites the emission of norepinephrine and suppressing the increase in stress blood pressure.



Pharmacokinetic data :

Absorption :

It presents a very rapid absorption with a maximum peaked concentration after the time of 2 hours. The distribution of Cilnidipine tends to be higher in the liver & in kidneys, plasma and other tissues. Cilnidipine does not present at a high accumulation in the tissue after repeated oral administration.

The Cilnidipine is reported to present at very low bioavailability determined to be about 13%. Tje low bioavailability is suggested to be due to its low aqueous solubility and the high permeability. Therefore efforts was made in order to find an innovative the formulation that can significantly improve the bioavailability of Cilnidipine . The formulations corresponds to generation of polymeric nanoparticles which enhance bioavailability .

Volume of distribution :

Drugs on the group of dihydropyridines such like cilnidipine tend to has a large volume of distribution.

Protein binding:

It presents the high protein binding that represents to 98% of the administered dose of drug.

Metabolism :

Cilnidipine can be metabolized in both liver and kidney. Tje Cilnidipine is rapidly metabolized by liver microsomes by the process of dehydrogenation.The major enzymatic isoform involved in cilnidipine drug dehydrogenation of dihydropyridine ring is CYP3A.

Route of elimination :

Cilnidipine can be eliminated through the urine in a proportion of 20 percent of the administered dose and 80 percent was eliminated by the feces.

Half-life :

The half-life of the hypotensive effect of cilnidipine is about 20 min.

Pharmacodynamics data :

Cilnidipine shows an antisympathetic profile in vitro and in vivo. Cilnidipine decreases blood pressure safely and effectively without excessive blood pressure reduction.

Materials and Methods

Characterizations of Drug polymer complex

The Drug polymer complex were studied by the method of Differential Scanning Calorimetry (DSC). The Thermal behavior of Cilnidipine was recorded using aDifferential Scanning Calorimeter.

Preparation of Orodispersible Tablets

Preliminary screening of superdisintegrants Orodispersible tablets containing Spray dried dispersion of Cilnidipine four superdisintegrants (Sodium starch glycolate, Crosscarmelose sodium, Cross povidone and Kyron T314) were prepared using direct compression method. The all essential ingredients as per formula were taken in mortar-pestle and mix well. Then it was compressed directly in rotary tablet compression machine.

Direct compression is a fast-dissolving tableting technique.

Except for all the materials were precisely weighed and put through the appropriate mass sieves before being uniformly mixed in a mortarand a tablet punching machine was used to compress the tablets.

Evaluation of Physical Parameters of Cilnidipine

The prepared solid dispersions were evaluated for various physical parameters which is mentioned below

1. Angle of repose
2. Carrs index
3. Hausners ratio
4. Particle size
5. Drug content uniformity
6. Hardness
7. Friability
8. Precompression parameters
9. Post compression parameters
10. Wetting time
11. Invitro disintegration studies
12. Stability studies

Angle of Repose

The flow properties of powder were determined to know the good or bad material flow. The powder was taken into a funnel and poured through it. Then a graph sheet was placed to form a heap like structure for which, the radius and height of the heap was measured. According to thos the angle of repose was calculated by using the formula

Angle of repose(θ)= $\tan^{-1}(h/r)$

Carr's Index

The Carr's index is a simple test used to evaluate the flow ability of a powder by comparing the poured density and the tapped density of a powder and the rate at which it is packed down

Carr's index= $\frac{\text{Tapped density – Poured density}}{\text{Tapped density}} \times 100$

Hausners ratio

It is used to evaluate flow properties of the powder .Hausner's ratio can be calculated by using the formula:

Hausners ratio= Tapped density/ Bulk density

Particle size

The particle size can be evaluated by using sieves a set of sieves were taken, properly cleaned and are stacked in descending order of mesh size. The solid was taken in the sieve number 18 The sieves are closed with lid and sieving was done for 5min.The material retained on individual sieves were collected and weighed

Drug content uniformity

The Solid dispersions of Clinidipine equivalent to 10 mg was weighed and transferred into a 100 ml volumetric flask.Small quantity of methanol was added to dissolve it was shaken occasionally for about 15 minutes and the volume was made up to 100 ml by using methanol. The solution was filtered by using Whattmann filter paper. The filtrate was subsequently diluted with 6.8pH phosphate buffer and the absorbance was measured at 240nm using 6.8pH phosphate buffer as blank.

Hardness

It is also known as crushing strength. The hardness is define as the force required to break the tablet in the radial direction was measured using Monsanto hardness tester. The force is applied to the edge of the tablet was gradually increased by moving the screw knob forward until the tablet breaks. The reading was noted from the scale which indicates the pressure required in kg/cm break the tablet.

Friability

Friability test was performedby using Roche frabilator. Ten tablets of a batch were weighted and placed in a friabilator chamber and it was allowed to rotate for 100 revolutions during each revolution these tablets falls from adistance of six inches to undergo shock. After completion of 100 revolutions, tablets were again weighed and the loss in weight indicated friability. The acceptance limits of weight loss should not be more than 1%. The friability test was performed to evaluate the ability of the tablets to withstand abrasion in packing, handling and transporting.

Precompression Parameters

It contains

- Bulk density,
- Tapped density,
- Compressibility index
- hausner's ratio,
- Angle of repose

Postcompression Studies

- Weight variation,
- Thickness,
- Diameter,
- Hardness,
- Friability,
- Assay

Wetting time

The wetting test is carried out by Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter.Ten ml of water containing Eosin (water-soluble dye) , is added to petridish.Then a tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is called as a wetting time.

Invitro disintegration studies

Disintegration time was determined using the disintegration apparatus USP in water maintaining the temperature at 37 ± 2°C.

Stability studies

The prepared orodispersible tablet was packed in Aluminum pouch and charged for short term stability studies at 40 °C and 75% RH for 1 month in a humidity chamber. Samples withdrawn after 1 month showed no significant change in appearance of tablets, % drug content, disintegration time, hardness and drug dissolution profile.

Conclusion

The study showed that cilnidipine's binary and ternary dispersions both provided faster rates of solubility than the drug in its pure form. The DSC and XRD analysis supported the hypothesis that the ternary system had a greater amorphizing effect than binary solid dispersion due to the presence of surfactant. The drug was better dissolved from the ternary dispersion systems due to the intermolecular interactions between the drug and carriers that improved drug dispersion in the polymer matrix, reduced drug particle size, increased amorphous nature, increased wettability, and decreased surface tension.We had concluded that the orodispersible tablets of Cilnidipine having a different evaluation parameters

- Angle of repose
- Carrs index
- Hausners ratio
- Particle size

- Drug content uniformity
- Hardness
- Bulk density,
- Tapped density,
- Compressibility index

For the betterment in Dissolution factor of drug the proportion of polymers plays important role.

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